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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
RAWLINGS, STEPHEN L	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 04/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/684,890	ZENTGRAF ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-16,18,23-25 and 30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *12* is/are allowed.

6)☒ Claim(s) *13-16, 18, 23-25, and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed February 11, 2005 is acknowledged and has been entered. Claims 17, 19-22, and 26 have been canceled. Claims 12, 13, 18, and 23-25 have been amended. Claim 30 has been added.

2. The affidavit under 37 C.F.R. § 1.132 by Prof. Dr. Angel Alonso filed February 11, 2005 is acknowledged and has been entered.

3. Claims 12-16, 18, 23-25, and 30 are pending in the application and are currently subject to prosecution.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. The following Office action contains NEW GROUNDS of rejection necessitated by amendment.

Grounds of Objection and Rejection Withdrawn

6. Unless specifically reiterated below, Applicant's amendment filed February 11, 2005 has obviated the grounds of objection and rejection set forth in the Office action mailed August 13, 2004.

Grounds of Objection Maintained

Amendment

7. The objection under 35 U.S.C. 132 to the amendment filed October 10, 2002, because it introduces new matter into the disclosure, is maintained.

As noted in section 7 of the previous Office action, the added material, which is not supported by the original disclosure, is the amino acid sequence of accession

number Y08612 and the nucleic acid sequence encoding the protein of accession number Y08612 at page 6.

In order to remedy this issue, the previous Office action suggested that Applicant to submit an affidavit or declaration executed by Applicant, or a practitioner representing Applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application.

In response to the previous Office action, Applicant has filed an affidavit under 37 C.F.R. § 1.132 by Prof. Dr. Angel Alonso, which states:

> I declare that the amino acid sequence of SEQ ID NO: 2 recited in the present claims 13, 23, and 24, and as presented in Applicants' Sequence Listing of October 7, 203, is identical in amino acid sequence to the sequence set forth as GenBank™ accession number Y08612 cited in Martinez *et al.*"

See also page 8 of the amendment, which addresses the merit of the affidavit.

The affidavit is not sufficient to overcome the objection because the affidavit does not state *that the amendatory material consists of the same material incorporated by reference in the referencing application*. It is understood that the amino acid sequence set forth as SEQ ID NO: 2 is presently the same as the amino acid sequence set forth as GenBank™ accession number Y08612; however, because sequences reported in GenBank™ are subject to change, it is not clear that the amino acid sequence that is identified in the originally filed specification as that disclosed as GenBank™ accession number Y08612 is the same as the sequence that is now set forth in the instant application as SEQ ID NO: 2.

It is noted that according to the annotations in GenBank™, on July 20, 1999, the present sequence version (i.e., Y08612.2, GI:5541878) replaced a previous sequence version (i.e., GI:1707521). The "Sequence Revision History" may be reviewed on the Internet at http://www.ncbi.nlm.nih.gov/entrez/. However, there does not appear to have been any substantive changes to the amino acid sequence since the filing date of the instant application, which suggests that the amendatory material consists of the same

material incorporated by the reference in the originally filed specification to the database accession number.

Nevertheless, it is again suggested that this issue be remedied by Applicant's submission of an affidavit or declaration executed by Applicant, or a practitioner representing Applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application.

Specification

8. The objection to the specification, because of the use of improperly demarcated trademarks in the specification, is maintained.

At page 6, Applicant has stated that the specification will be amended to ensure that any disclosed trademarks are appropriately demarcated when this application is in condition for allowance.

As a matter of formality, this application will not be in condition for allowance unless and until this issue has been remedied by appropriate amendment to the specification.

Grounds of Rejection Maintained

Claim Rejections - 35 USC § 112

9. The rejection of claims 13-16, 18, 23-25, and 30 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is maintained. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a new matter rejection, the ground of which is set forth in section 10 of the previous Office action.

At page 8 of the amendment filed February 11, 2005, Applicant has traversed this ground of rejection upon the merit of the affidavit under 37 C.F.R. § 1.132 by Prof. Dr. Angel Alonso.

The merit of the affidavit has been carefully considered but not found sufficient to overcome this ground of rejection for the reasons set forth above in section 7.

10. The rejection of claims 13-16, 18, and 30 under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for using** a method for identifying the presence of a malignant tumor in a tissue biopsy sample comprising:

(a) determining the amount of the polypeptide of SEQ ID NO: 2 using the antibody deposited under accession number DSM ACC 2457, a monoclonal antibody that binds the polypeptide of SEQ ID NO: 2, or a recombinant or chimeric molecule comprising each of the six CDRs of the monoclonal antibody bearing the accession number DSM ACC 2457 or

(b) determining the amount of a transcript encoding said polypeptide using an oligonucleotide that binds the transcript encoding said polypeptide,

whereby the presence of malignant tumor is identified if said amount is greater than the amount in normal control tissue, **does not reasonably provide enablement for using** a method for identifying the presence of a benign tumor in a tissue biopsy sample, or a method for identifying the presence of a malignant tumor in a tissue biopsy sample comprising determining the amount of the polypeptide of SEQ ID NO: 2 using an antibody that does not bind the polypeptide of SEQ ID NO: 2, is maintained. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The ground of this "scope of enablement" rejection set forth in section 13 of the previous Office action.

At page 10 of the amendment filed February 11, 2005, Applicant has traversed this ground of rejection.

Applicant's arguments has been carefully considered but not found persuasive for the following reasons:

Upon careful consideration of the factors used to determine whether undue experimentation is required, in accordance with *Ex parte Forman*, 230 USPQ 546 (BPAI

1986), and in view of a preponderance of factual evidence of record, the amount of guidance, direction, and exemplification disclosed in the specification would not be sufficient to enable the skilled artisan to use the claimed invention without undue experimentation.

As explained at page 12 of the previous Office action, the specification discloses that "cancer cells" include the cells of benign tumors, which the specification discloses cannot be detected using the claimed invention. Gould et al. (of record) has been cited in further support of this issue.

With regard to claim 30, only a monoclonal antibody that binds the polypeptide of SEQ ID NO: 2 can be used in practicing the claimed invention without undue experimentation. At present, claim 30 in not interpreted to limit the monoclonal antibody to a monoclonal antibody that binds the polypeptide of SEQ ID NO: 2. It is therefore suggested that the claim be amended to recite, for example, "(i) a monoclonal antibody that binds to the protein and (ii) a recombinant or chimeric [...]".

In response to Applicant's argument, despite the fact that the claims 13-16, 18, and 23-25 are limited to methods that use the deposited antibody, for the reasons set forth in the previous Office action, even the deposited antibody cannot be used without undue experimentation to practice the claimed method for identifying the presence of any tumor in a tissue biopsy sample, since the method cannot be used to detect *benign* tumors. Similarly, claim 30, which as explained is not limited to a method that uses the deposited antibody, is not reasonably enabled by the supporting disclosure, since the skilled artisan could not use an antibody that binds the polypeptide of SEQ ID NO: 2 to detect the presence of a benign tumor cell without undue experimentation, if at all.

11. The rejection of claims 23-25 under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for making and using** a kit for diagnosing a malignant tumor, **does not reasonably provide enablement for making and using** a kit for diagnosing *any* tumor, including a benign tumor, is maintained. The specification does not enable any person skilled in the art to which it pertains, or with which it is most

nearly connected, to make and use the invention commensurate in scope with these claims.

The ground of this "scope of enablement" rejection set forth in section 14 of the previous Office action.

At page 11 of the amendment filed February 11, 2005, Applicant has traversed this ground of rejection.

Applicant's arguments has been carefully considered but not found persuasive for the following reasons:

With all due respect, the previous Office action does not state that the supporting disclosure is enabling for making and using the claimed invention for diagnosing cancer. As explained above, the claimed invention cannot be used to diagnose benign "cancer cells" without undue experimentation, since it appears that the expression of the gene encoding Nup88 (i.e., the polypeptide of SEQ ID NO: 2 is not diagnostic or indicative of benign tumors.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

12. Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Martinez et al. (*Cancer Res.* **59**: 5408-5411, 1999) (of record) in view of Campbell (Monoclonal Antibody Technology, Laboratory Techniques in Biochemistry and Molecular Biology, Elsevier Science Publishers B.V.: Amsterdam, The Netherlands, Vol. 13, pp. 1-32).

Claim 30 is drawn to a method for identifying the presence of a cancer cell comprising providing a tissue biopsy sample and determining the level of expression of the polypeptide of SEQ ID NO: 2 in the sample by annealing a nucleic acid molecule that specifically binds a transcript encoding said polypeptide to said transcript.

Martinez et al. teaches that which is set forth in sections 18 and 21 of the previous Office action. In particular, Martinez et al. teaches analyzing tissue biopsy samples to determine if the polypeptide of SEQ ID NO: 2, i.e., Nup88, is overexpressed in malignant ovarian tissue, as compared to healthy adjacent tissue; see entire document (e.g., the abstract). Martinez et al. teaches a polyclonal antibody that binds

Nup88 (page 5408, column 1), which can be used to make the determination by immunohistochemical methods; see, e.g., page 5410, column 1.

Martinez et al., however, does not expressly teach a monoclonal antibody that binds the polypeptide of SEQ ID NO: 2, or the use of the disclosed method for idenrtifying the presence of a cancer cell comprising measuring the level of expression of the protein using such a monoclonal antibody.

Campbell teaches monoclonal antibodies can be used advantageously, compared to polyclonal antibodies; see entire document. For example, Campbell teaches that monoclonal antibodies have increased specificity, relative to polyclonal antisera; see, e.g., pages 5-7. Moreover, Campbell teaches it is "customary now for any group working on a macromolecule to [...] make monoclonal antibodies to it (sometimes without a clear objective for their application)" (page 29).

Accordingly, it would have been *prima facie* obvious to one ordinarily skilled in the art at the time of the invention to produce a monoclonal antibody for use in determining the level of expression of Nup88 in tissue biopsy samples, since monoclonal antibodies bind more specifically to an antigen than polyclonal antisera. One ordinarily skilled in the art at the time of the invention would have been motivated to do so to identify the presence of cancer cells in a tissue biopsy sample.

Conclusion

13. Claim 12 has been allowed; no other claims are allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
April 1, 2005

LARRY R. HELMS, PH.D
PRIMARY EXAMINER